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NOTICE OF ALLOWANCE AND FEE(S) DUE

22511 7590 07/08/2008

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1221 MCKINNEY STREET
SUITE 2800
HOUSTON, TX 77010

EXAMINER	
TUCKER, ZACHARY C	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/08/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,009	01/30/2006	Serguei Sviridov	17243/006001	9901

TITLE OF INVENTION: PIPERAZINE DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1440	$300	$0	$1740	10/08/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

22511 7590 07/08/2008

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,009	01/30/2006	Serguei Sviridov	17243/006001	9901

TITLE OF INVENTION: PIPERAZINE DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1440	$300	$0	$1740	10/08/2008

EXAMINER	ART UNIT	CLASS-SUBCLASS
TUCKER, ZACHARY C	1624	514-252110

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☐ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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TUCKER, ZACHARY C	
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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 362 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 362 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	10/567,009	SVIRIDOV ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *30 May 2008*.

2. ☒ The allowed claim(s) is/are *4-9,29-35,37,46-49,51,52 and 55-59*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Art Unit: 1624

EXAMINER'S AMENDMENT

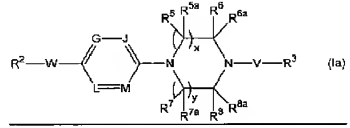
An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in an e-mail exchange between the examiner and applicants' counsel, Dr. T. Chiyau Liang, on 30 May, 2 June and 3 June, 2008:

The claims have been amended as shown:

Claims 1-3, 10-28. 36. 38-45. 50, 53 and 54 have been cancelled.

4. (Currently Amended) A method of treating a disease or condition mediated by stearoyl-CoA desaturase (SCD) in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (Ia):



(Ia)

wherein:

x and y are each independently 1, 2 or 3;

W is -N(R^1)C(O)N(R^1)-, -O-, -N(R^1)-, -S(O)$_t$- (where t is 0, 1 or 2), -N(R^1)S(O)$_2$-, -S(O)$_2$N(R^1)-, -C(O)O- or -N(R^1)C(O)O-;

W is -N(R^1)C(O)N(R^1)-, -O-, -N(R^1)-, -S(O)$_t$- (where t is 0, 1 or 2), -N(R^1)S(O)$_2$-, -S(O)$_2$N(R^1)-, -C(O)O- or -N(R^1)C(O)O-;

V is -C(O)-, -C(O)O-, -C(S)-, -C(O)N(R^1)-, -S(O)$_2$-, or -S(O)$_2$N(R^1)-;

G and M are each -N=, and J and L are each -C(R^4)=;

each R^1 is independently selected from the group consisting of hydrogen, C$_1$-C$_{12}$alkyl, C$_2$-C$_{12}$hydroxyalkyl, C$_6$-C$_{12}$cycloalkylalkyl and C$_7$-C$_{19}$aralkyl;

R^2 is selected from the group consisting of C$_1$-C$_{12}$alkyl, C$_2$-C$_{12}$alkenyl, C$_2$-C$_{12}$hydroxyalkyl, C$_2$-C$_{12}$hydroxyalkenyl, C$_2$-C$_{12}$alkoxyalkyl, C$_3$-C$_{12}$cycloalkyl, C$_3$-C$_{12}$cycloalkylalkyl, aryl, C$_7$-C$_{19}$aralkyl, C$_3$-C$_{12}$heterocyclyl, C$_3$-C$_{12}$heterocyclylalkyl, C$_1$-C$_{12}$heteroaryl, and C$_3$-C$_{12}$heteroarylalkyl;

or R^2 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R^3 is selected from the group consisting of C$_1$-C$_{12}$alkyl, C$_2$-C$_{12}$alkenyl, C$_2$-C$_{12}$hydroxyalkyl, C$_2$-C$_{12}$hydroxyalkenyl, C$_2$-C$_{12}$alkoxyalkyl, C$_3$-C$_{12}$cycloalkyl, C$_4$-C$_{12}$cycloalkylalkyl, aryl, C$_7$-C$_{19}$aralkyl, C$_3$-C$_{12}$heterocyclyl, C$_3$-C$_{12}$heterocyclylalkyl, C$_1$-C$_{12}$heteroaryl and C$_3$-C$_{12}$heteroarylalkyl;

or R^3 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

each R^4 is independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-N(R^9)_2$;

each R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} is independently selected from hydrogen or C_1-C_3alkyl;

or R^5 and R^{5a} together, or $R^6$and R^{6a} together, or $R^7$and R^{7a} together, or R^8 and R^{8a} together are an oxo group, provided that when V is -C(O)-, $R^6$and R^{6a} together or R^8 and R^{8a} together do not form an oxo group, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl;

or one of R^5, R^{5a}, R^8, and R^{8a} together with one of R^7, R^{7a}, R^8 and R^{8a} form an alkylene bridge, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8, and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl;

R^{10} is hydrogen or C_1-C_3alkyl; and

each R^9 is independently selected from hydrogen or C_1-C_3alkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof,

wherein the mammal is a human.

~~The method of Claim 3~~ wherein the disease or condition is selected from the group consisting of fatty liver, non-alcoholic steatohepatitis, Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, dyslipidemia, acne, and metabolic syndrome and any combination of these.

5. (Original) The method of Claim 4 wherein the disease or condition is Type II diabetes.

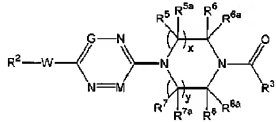
6. (Original) The method of Claim 4 wherein the disease or condition is obesity.

7. (Original) The method of Claim 4 wherein the disease or condition is metabolic syndrome.

8. (Original) The method of Claim 4 wherein the disease or condition is fatty liver.

9 (Original) The method of Claim 4 wherein the disease or condition is non-alcoholic steatohepatitis.

20. (Currently Amended) A compound of formula (III):



(III)

wherein:

x and y are each independently 1, 2 or 3;

W is -N(R^1)C(O)-, -C(O)N(R^1)- or -OC(O)N(R^1)-;

G and M are each -C(R^4)=;

each R^1 is independently selected from the group consisting of hydrogen C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{16}aralkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_3-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_7-C_{16}aralkyl, C_2-C_{12} heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

or R^2 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R^3 is phenyl optionally substituted by one or more substituents selected from the

group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{12}$, $-C(O)OR^{12}$, $-S(O)_2N(R^{12})_2$, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl, provided that R^3 is not phenyl substituted with optionally substituted thienyl

each R^4 is independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-N(R^5)_2$;

each R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} is independently selected from hydrogen or C_1-C_3alkyl;

or R^5 and R^{5a} together or R^7 and R^{7a} together form an oxo group, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl;

or one of R^6, R^{6a}, R^8, and R^{8a} together with one of R^7, R^{7a}, R^8 and R^{8a} form an alkylene bridge, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8, and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl;

each R^9 is independently selected from hydrogen or C_1-C_6alkyl; and

each R^{12} is independently selected from hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof~~, a pharmaceutical composition thereof or a prodrug thereof~~.

30. (Original) The compound of Claim 29 wherein W is $-N(R^1)C(O)-$.

31. (Original) The compound of Claim 30 wherein:

x and y are each 1;

R^1 is hydrogen or C_1-C_6alkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_3-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_7-C_{15}aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{12}$, $-C(O)OR^{12}$, $-S(O)_2N(R^{12})_2$, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl, provided that R^3 is not phenyl substituted with optionally substituted thienyl;

each R^4 is hydrogen;

each R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} is hydrogen; and

each R^{12} is independently selected from hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl.

32. (Original) The compound of Claim 31 wherein:

R^2 is independently selected from C_2-C_{12}alkenyl or C_1-C_{12}alkyl optionally substituted by -OR^{12};

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy; and

R^{12} is hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl.

33. (Original) The compound of Claim 32 selected from the group consisting of the following:

4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid (3-methyl-butyl)-amide;

4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid (2-phenoxy-ethyl)-amide; and

4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid pentylamide.

34. (Original) The compound of Claim 31 wherein:

R^2 is C_7-C_{12}aralkyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_8alkyl and C_1-C_8trihaloalkyl; and

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C_1-C_8alkyl, C_1-C_8trihaloalkyl and C_1-C_8trihaloalkoxy.

35. (Original) The compound of claim 34 selected from the group consisting of the following:

4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid phenethyl-amide;

4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid (3-phenyl-propyl)-amide;

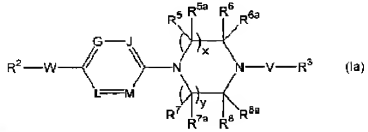
4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid [2-(4-fluoro-phenyl)-ethyl]-amide;

4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid [3-(4-fluoro-phenyl)-propyl]-amide; and

4-(2-Trifluoromethyl-benzoyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid [3-(4-fluoro-phenyl)-propyl]-amide.

37. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of Claim 29.

46. (Currently Amended) A compound of formula (Ia):



(Ia)

wherein:

x and y are each independently 1, 2 or 3;

W is $-N(R^1)C(O)N(R^1)-$, -O-, $-N(R^1)-$, $-S(O)_t-$ (where t is 0, 1 or 2), $-N(R^1)S(O)_2-$, $-S(O)_2N(R^1)-$, $-C(C)O-$ or $-N(R^1)C(O)O-$;

V is -C(O)-, -C(O)O-, -C(S)-, $-C(O)N(R^1)-$, $-S(O)_2-$ or $-S(O)_2N(R^1)-$;

G and M are each -N=, and J and L are each $-C(R^4)=$

~~**G, J, L and M are each independently selected from -N= or $-C(R^4)=$; provided that at least two of G, J, L and M are -N=, and provided that when G and J are both $-C(R^4)=$, L and M can not both be -N=, and when L and M are both $-C(R^4)=$, G and J can not both be -N=**~~;

each R^1 is independently selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{16}aralkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl, C_7-C_{16}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl, and C_3-C_{12}heteroarylalkyl;

or R^2 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R^3 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalky , C_2-C_{12}hydroxyalkenyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl, C_7-C_{16}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

or R^3 is a multi-ring structure having 2 to 4 rings wherein the rings are

independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

each R^4 is independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-N(R^a)_2$;

each R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} is independently selected from hydrogen or C_1-C_3alkyl;

or R^5 and R^{5a} together, or R^6 and R^{6a} together, or R^7 and R^{7a} together, or R^4 and R^{4a} together are an oxo group, provided that when V is -C(O)-, R^6 and R^{6a} together or R^8 and R^{8a} together do not form an oxo group, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl;

or one of R^5, R^{5a}, R^6, and R^{6a} together with one of R^7, R^{7a}, R^8 and R^{8a} form an alkylene bridge, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8, and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl; and

each R^9 is independently selected from hydrogen or C_1-C_6alkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof, ~~a pharmaceutical composition thereof or a prodrug thereof~~.

47. (Original) The compound of Claim 46 wherein W is $-N(R^1)C(O)N(R^1)-$ and V is -C(O)-.

48. (Original) The compound of Claim 47 wherein:

x and y are each 1;

each R^1 is independently selected from the group consisting of hydrogen or C_1-

C_6alkyl;

R^2 s selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl, C_7-C_{18}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl, and C_3-C_{12}heteroarylalkyl;

R^3 s selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_2-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, aryl, C_7-C_{18}aralkyl, C_3-C_{12}heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl;

each R^4 is hydrogen; and

each R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} is hydrogen.

49. (Original) The compound of Claim 48 wherein:

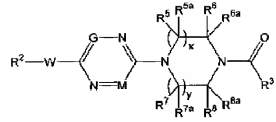
R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_4-C_{12}cycloalkylalkyl, C_7-C_{18}aralkyl, C_3-C_{12}heterocyclylalkyl and C_3-C_{12}heteroarylalkyl;

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{12}$, $-C(O)OR^{12}$, $-S(O)_2N(R^{12})_2$, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each R^{12} is independently selected from hydrogen, C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl.

51. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of Claim 46

52. (New) A method of treating a disease or condition mediated by stearoyl-CoA desaturase (SCD) in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (III):



(III)

wherein:

x and y are each independently 1, 2 or 3;

W is $-N(R^1)C(O)-$, $-C(O)N(R^1)-$ or $-OC(O)N(R^1)-$;

G and M are each $-C(R^4)=$;

each R^1 is independently selected from the group consisting of hydrogen, C_1-C_{12}alkyl, C_2-C_{12}hydroxyalkyl, C_4-C_{12}cycloalkylalkyl and C_7-C_{19}aralkyl;

R^2 is selected from the group consisting of C_1-C_{12}alkyl, C_2-C_{12}alkenyl, C_2-C_{12}hydroxyalkyl, C_2-C_{12}hydroxyalkenyl, C_3-C_{12}alkoxyalkyl, C_3-C_{12}cycloalkyl, C_4-C_{12}cycloalkylalkyl, C_7-C_{19}aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12}heterocyclylalkyl, C_1-C_{12}heteroaryl and C_3-C_{12}heteroarylalkyl,

or R^2 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R^3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1-C_8alkyl, C_1-C_8trihaloalkyl, C_1-C_8trihaloalkoxy, C_1-C_8alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{12}$, $-C(O)OR^{12}$, $-S(O)_2N(R^{12})_2$, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl, provided that R^3 is not phenyl substituted with optionally substituted thienyl;

each R^4 is independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-N(R^5)_2$;

each R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} is independently selected from hydrogen or C_1-C_3alkyl;

or R^5 and R^{5a} together or $R^7$and R^{7a} together form an oxo group, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8 and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl;

or one of R^5, R^{5a}, R^8, and R^{8a} together with one of R^7, R^{7a}, R^6 and R^{6a} form an alkylene bridge, while the remaining R^5, R^{5a}, R^6, R^{6a}, R^7, R^{7a}, R^8, and R^{8a} are each independently selected from hydrogen or C_1-C_3alkyl;

each R^9 is independently selected from hydrogen or C_1-C_6alkyl; and

each R^{12} is independently selected from hydrogen, C_1-C_8alkyl, C_3-C_8cycloalkyl, aryl or aralkyl;

a stereoisomer, enantiomer or tautomer thereof, or a pharmaceutically acceptable salt thereof

, wherein the mammal is a human, wherein the disease or condition is selected from the group consisting of fatty liver, non-alcoholic steatohepatitis, Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, dyslipidemia, acne, and metabolic syndrome and any combination of these.

55. The method of claim ~~54~~ 52 wherein the disease or condition is Type II diabetes.

56. The method of claim ~~54~~ 52 wherein the disease or condition is obesity.

57. The method of claim ~~54~~ 52 wherein the disease or condition is metabolic syndrome.

58. The method of claim ~~54~~ 52 wherein the disease or condition is fatty liver.

59. The method of claim ~~54~~ 52 wherein the disease or condition is non-alchoholic steatohepatitis.

end of amendments

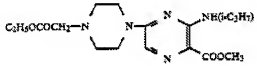
Art Unit: 1624

Lack of Unity of Invention

In view of the present amendments, the finding of lack of unity of invention between compounds as were set forth in Group X of the previous Office action, and methods of using those compounds (Group III), is hereby withdrawn. Claims of Group III are hereby rejoined.

Compounds according to claims 29-35, and claim 37, the pharmaceutical composition comprised thereof, described, claims 46-49 and claim 51, drawn to a pharmaceutical composition comprised thereof, and methods according to instant claims 4-9 and 52-59 are novel nor are they obvious over the prior art. The attached Examiner's Amendment places the claims in condition for allowance.

The closest prior art with respect to the compounds according to the invention, *per se*, comes from: US 4,959,368 (Awaya et al), which discloses therapeutic agents for neurological diseases. Compound #100, at the top of the table beginning on columns 7 and 8 of the patent, has a structure represented by the following diagram:



but is excluded from the scope of the instant claims by virtue of there not being a group corresponding to "V" in the structure.

The state of the art, at the time the present invention was made, with respect to the therapeutic application of inhibitors of stearoyl-CoA-desaturase is well-taught by the following reference:

Ntambi & Miyazaki "Recent insights into stearoyl-CoA desaturates -1" *Current Opionion in LIpidology*, vol. 14, pages 255-261 (2003).

Ntambi & Miyazaki teach that inhibitors of Stearoyl-CoA desaturase-1 is a central lipogenic enzyme catalyzing the introduction of double bonds into the saturated structure of mainly oleic acid (page 255, top of paragraph one). This activity has implications in the signaling of upregulation of lipid production in animials fed a high carbohydrate diet (page 256, under "Role of SCD1 in lipid biosynthesis"

Studies in SCD$^{-/-}$ mice show that the animals have very low levels of hepatic triglycerides and cholesterol esters, even when fed a lipogenic diet. This results in reduced adipose tissue in these animals, and thus, increased insulin sensitivity (improved glucose tolerance).

Ntambi & Miyazaki conclude that SCD1 represents a "bottleneck" in triglyceride synthesis and is responsible for the development of the obese phenotype of *ob/ob* mice. The article concludes that SCD1 is a component of the novel metabolic response to leptin signaling and therefore appears to be a promising therapeutic target that could be used in the treatement of obesity, diabetes, and other metabolic diseases.

Thus, in light of the teachings of Ntambi & Miyazaki, the methods according to instant claims 4-9 and 52-59 are deemed to be enabled by the disclosure.

Allowable Subject Matter

Claims 4-9, 29-35, 37, 46-49, 51, 52 and 55-59 are allowed, as they are deemed free of the prior art and enabled by the disclosure.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Art Unit: 1624

Conclusion

All Post-Allowance Correspondence concerning this application must be mailed to:

Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Or you can fax them to the Office of Patent Publications at 703-872-9306, in order to expedite the handling of such correspondence as amendments under 37 CFR 1.312; information disclosure statements, and formal drawings. Sending Post-Allowance papers to Technology Center 1600 will only cause delays in matching papers with the case.

For information concerning status of correspondence sent after receipt of the Notice of Allowance, please contact the Correspondence Branch at (703) 305-8027. The Notice of Allowance also has an insert containing contact information on other items, including Issue Fees, receipt of formal drawings and the status of the application.

/Zachary C. Tucker/
Primary Examiner
Art Unit 1624